Remarks:

Reconsideration of the application is respectfully requested in view of the foregoing amendments and following remarks. Claims 1-5, 7-40 and 64-68 are pending in the application. Claims 15-40 have been withdrawn. No claims have been allowed. Claims 1, 64, and 68 are independent.

Cited Art

U.S. Patent No. 5,817,462 to Garini et al. ("Garini") is entitled "method for simultaneous detection of multiple fluorophores for in situ hybridization and multicolor chromosome painting and banding." U.S. Patent No. 5,784,162 to Cabib et al. ("Cabib") is entitled "Spectral bio-imaging methods for biological research, medical diagnostics and therapy."

Interview Summary

Applicants thank the Examiner for his time during an interview on July 12, 2005. During the interview, Applicants discussed claim 1 and Garini. Agreement was reached regarding various issues. However, the Examiner indicated that an updated search or additional consideration of Garini would be done.

Election/Restrictions

The Action found that claims 15-40 were drawn to a nonelected species and, therefore, withdrew them from further consideration. Applicants believe, as is discussed below, that claim 1 is allowable in its present form.

The Office Action of January 4, 2005 identified claims 1-14 as generic. Because generic claim 1 is allowable, and claims 15-40 depend upon claim 1, claims 15-40 and are also allowable. Therefore, Applicants respectfully request that the Examiner withdraw the species and subspecies election requirements on claims 15-40, and continue to consider those claims for allowance.

Patentability of Claims 1-6, 10, 11, 13, 14, and 64-66 over Garini under §102(e)(2)

Claims 1-6, 10, 11, 13, 14 and 64-66 stand rejected under § 102(e)(2) over Garini. Applicants have amended claims 1 and 64 by adding language from claim 6 and also clarify by adding "spatially" before "overlapping." The language "nucleic acid probe" has been added between "overlapping" and "signals" to further clarify. Some of the changes merely clarify terms in the original language of claim 6; the amendment does not necessarily narrow the claimed scope. As pointed out below, no new matter is added thereby.

Claim 1

Claim 6 is cancelled. The language of claim 6 is now incorporated into claim 1, so the rejection of claim 6 will be discussed in the following arguments for claim 1.

Amended claim 1 recites in relevant part a method comprising "with the plurality of successive images of the region of interest, distinguishing spatially overlapping nucleic acid probe signals in the biological specimen...." For example, the specification describes at page 2, line 29 et seq.:

> "A significant impediment to the accurate counting of fluorescent signals is that the probes hybridize throughout a three-dimensional nucleus, and the probe signals have to be counted from different focal planes for each nucleus. However, cells and probe signals can overlap in the two-dimensional view, and overlapping signals are seen as a single signal. Such overlapping results in undercounting of signals, which can make it appear that an amplified gene is less amplified, or that fewer copies of a normal gene are present."

See also figures 1A and 1B for graphical depictions of "spatially overlapping nucleic acid probe signals."

For a 102(e) rejection to be proper, the cited art must show each and every element as set forth in a claim. (See MPEP § 2131.01.) However, the cited art does not so show.

Garini's description of a means of improving the signal-to-noise ratio in fluorescence microscopy does not anticipate the recited "distinguishing spatially overlapping nucleic acid probe signals." Garini describes at column 23, line 7 et seq.:

> In spite of the best filtering methods available, undesirable background luminescence makes it often difficult, and sometimes impossible, to bring out the relevant fluorescence signal from its

> background (noise). The spectral bio-imaging method of the present invention is able, on the other hand, to use spectral differences between (i) the spectral shape and spectral range of the fluorescent dye and (ii) the spectral shape and spectral range of the background luminescence (including auto-fluorescence), to eliminate the effects of undesirable background luminescence.
>
> Thus by applying the appropriate spectral image analysis methods to the emission spectra of fluorescent probes, it is possible to improve the signal-to-noise ratio, and hence the accuracy, of fluorescence imaging measurements.

Thus Garini does describe "bring[ing] out the relevant fluorescence signal from its background (noise)." However, bringing out a relevant signal from its background does not anticipate the recited "distinguishing spatially overlapping nucleic acid probe signals." Because Garini does not teach each and every element of claims 1 and 64, those claims are patentable over Garini.

Accordingly, claim 1 and its dependent claims 2-5, 7-14, and 65-67 are patentable over Garini.

Furthermore, claims 2-5, 7-14, and 65-67 each recite patentably-distinct subject matter not taught by Garini. Thus these claims are separately patentable.

Claim 68

New Claim 68 mimics the language of claim 1 and is therefore also allowable. Support for "computer-readable media" is found, for example, at Page 15, line 1 of the Application.

Claim 64

Amended claim 64 recites in relevant part "...distinguishing spatially overlapping nucleic acid probe signals...." Garini does not teach "distinguishing spatially overlapping nucleic acid probe signals." Therefore, claim 64 is also allowable over Garini.

Patentability of Claims 1-14 and 64-67 over Garini et al. taken in view of Cabib et al. under § 103

The Action rejects claims 1-14 and 64-67 under 35 U.S.C. § 103(a) as unpatentable over Garini taken in view of Cabib. Applicants respectfully submit the claims in their present form are allowable over the cited art. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation

of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (MPEP § 2142.)

Cabib's discussion of "specific depths of the cell" fails to teach or suggest the recited "distinguishing overlapping probe signals." As Garini also fails to mention this feature, or provide sufficient motivation to modify Cabib to result in said feature, the claim is allowable over Carini taken in view of Garini. Cabib describes at column 38, line 47 et seq. (emphasis added):

> On the basis of these spectral imaging results of May-Grunwald-Giemsa stained cells, it is obvious that each point (or what is defined as a pixel) has its specific absorbance and transmittance spectra which can be classified into several categories. At this stage of research, there are some indications for a spectral component which may correlate well with what is called "the purple Romanowsky-Giemsa complex". The absorbance spectra of heterochromatin (FIG. 10c) shows clearly an outstanding absorbance peak at 540 nm which is in good accordance with what was described as the "purple Romanowsky-Giemsa complex" see, Friedrich et al. (1990) Histochemistry 93, pp. 247-256; Bottiroli et al. (1994) Lasers in Surgery and Medicine; Profio (1984) IEEE Journal of Quantum Electronics QE-20 pp. 1502-1506; Herman (1989) Fluorescence Microscopy of Living Cells in Culture, part B, Chapter 8, pp. 219-243, edited by Taylor and Wang, Academic Press Inc. (1989); and, Jovin and Arndt-Jovin (1989) Cell structure and function by microspectrofluorometry, Chapter 5, Academic Press Inc. The spectral cytoplasmic features (spectrum B of FIG. 9a), when used for similarity mapping, allow the clear demarcation of components which one believe represent the nuclear envelope, Golgi cisternae, cytoplasmic vacuoles, and the outer cell membrane. Nevertheless, stained cells, dried in the air, may show a superposition of cytoplasmic layers which apparently reduce resolution. For the future development of spectral imaging, the use of aldehyde-fixed cells which will enable to focus on *specific depths of the cell* and thus to markedly enhance the possibilities of this technique, is suggested.

Thus, Cabib does describe "specific depths of the cell." However, a mere description of "specific depths of the cell" would not lead one to the recited "distinguishing spatially overlapping nucleic acid probe signals."

Motivations to combine or modify references must come from the references themselves or be within the body of knowledge in the art. (*See* MPEP § 2143.01.)

Garini reads at column 5, line 16 et seq.:

> In a continuation application (U.S. Pat. No. 5,784,162 to Cabib et al., filed Dec. 12, 1995, which is incorporated by reference as if fully set forth herein) the objective was to provide spectral imaging methods for biological research, medical diagnostics and therapy, which methods can be used to detect spatial organization (i.e., distribution) and to quantify cellular and tissue natural constituents, structures, organelles and administered components such as tagging probes (e.g., fluorescent probes) and drugs using light transmission, reflection, scattering and fluorescence emission strategies, with high spatial and spectral resolutions. In U.S. Pat. No. 5,784,162, the use of the spectral imaging apparatus described in U.S. Pat. No. 5,539,517 for interphase fluorescent in situ hybridization of as much as six loci specific probes (each loci located on a different chromosome) was demonstrated, as well as additional biological and medical applications.
>
> In a continuation application (U.S. Pat. application Ser. No. 08/575,191, to Cabib et al., filed Dec. 20, 1995, which is incorporated by reference as if fully set forth herein) the objective was to provide a method for simultaneous detection of multiple fluorophores for detecting and analyzing fluorescent in situ hybridizations employing numerous chromosome paints and/or loci specific probes, each labeled with a different fluorophore or a combination of fluorophores. The method according to this invention is highly sensitive both in spatial and spectral resolutions and is capable of simultaneous detection of dozens of fluorophores and/or combinations of fluorophores, therefore it can be used for the detection of fluorescently painted complete sets of chromosomes and/or multiple loci from a species such as human and to provide a complete color karyotype.

While the Examiner has referenced language that shows that Cabib "is incorporated by reference as if fully set forth [in Garini]," Applicants cannot find within either of the references sufficient motivation to combine or modify that would result in the claimed arrangement.

For example, Applicants have also reviewed the Action's references to Cabib column 14, line 14 et seq., Cabib column 19, line 28 et seq., and Cabib column 7, line 53 et seq. In the interest of brevity, Applicants note that these passages similarly fail to teach or suggest the recited "distinguishing spatially overlapping nucleic acid probe signals."

Accordingly, claim 1 and its dependent claims, 2-5, 7-14, and 65-67, are patentable over Garini taken in light of Cabib. Claims 64 and new claim 68 are similarly allowable.

Furthermore, claims 2-5, 7-14, and 65-67 each recite patentably-distinct subject matter not taught or suggested by Garini taken in light of Cabib. Thus these claims are separately patentable.

Request for Interview

If any issues remain, the Examiner is formally requested to contact the undersigned attorney prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. Applicants submit the foregoing formal Amendment so that the Examiner may fully evaluate Applicants' position, thereby enabling the interview to be more focused.

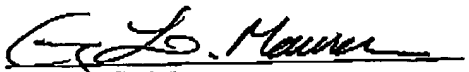
This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by a written request.

Conclusion

The claims in their present form should now be allowable. Such action is respectfully requested.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 
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